Ethnic differences in risk of compulsory psychiatric admission among representative cases of psychosis in London

Sara Davies, Graham Thornicroft, Morven Leese, Andrew Higgingbotham, Michael Phelan

Abstract

***Objective*—To compare the risk of detention under the Mental Health Act 1983 in a representative group of people with psychotic disorders from different ethnic groups.**

***Setting*—Two defined geographical areas in south London.**

***Design*—Annual period prevalent cases of psychosis were identified in 1993 in the study areas from hospital and community data. Standardised criteria were applied to case notes to establish diagnosis and detention under the act.**

***Subjects*—535 patients were identified, of whom 439 fulfilled ICD-10 criteria for psychosis.**

***Main outcome measures*—Risk of ever having been detained under the Mental Health Act 1983, risk of detention under specific sections of the act during the study year, and risk of contact with forensic services for the different ethnic groups.**

***Results*—439 patients with a psychotic illness were identified. Nearly half of the white patients had been detained under the act compared with 70% and 69% of black Caribbean and black African patients, respectively. Black Caribbean and black African patients were more likely than white patients to have been involuntarily detained (adjusted odds ratio 3·67; 95% confidence interval 2·07 to 6·50 and 2·88; 1·04 to 7·95, respectively). Rates of use of sections 2, 3, and 136 in the study year were higher for black than for white patients, and black patients were more likely than white patients to have been admitted to a psychiatric intensive care facility or prison.**

***Conclusion*—Independent of psychiatric diagnosis and sociodemographic differences, black African and black Caribbean patients with psychosis in south London were more likely than white patients to have ever been detained under the Mental Health Act 1983.**

Introduction

A high prevalence of severe mental illness, particularly schizophrenia, has been reported among black Caribbean people in Britain.[1-6] This contrasts with lower rates of psychosis found among Irish people[7] and conflicting results in Asian populations.[2 8 9] Furthermore, high rates of hospital admission under the Mental Health Act 1983 have been reported for black Caribbean patients, particularly young men,[10-13] both for compulsory admissions involving the police[12 14] and for forensic orders.[6 15] Independent of diagnosis, black Caribbean patients seem more likely to have contact with the police and forensic services,[6] to be treated in intensive care facilities if detained under the act,[16] and to have had a criminal conviction if they are young and male.[17]

Previous studies differ regarding whether the increased rate of compulsory admissions for black Caribbeans can be explained by an increased incidence of schizophrenia or other psychosis[8 12 13] or whether it results from diagnostic bias[14] or is an independent finding.[6 13 16] Compulsory admission is more likely in patients who are living in temporary accommodation, in those not registered with a general practitioner, those attending a psychiatric outpatient department, and those with previous admissions.[15] There are also major diagnostic differences between compulsory and non-compulsory admissions, with diagnoses of schizophrenia and mania overrepresented and depression underrepresented in the compulsory admissions group.[13]

When the increased compulsory admission rates have been shown to be an independent finding, explanations have been proposed which are either "patient" or "service" based.[18] Such high rates may be attributable to different types of schizophrenia in this population,[19] different perceptions of health services by black Caribbean patients, or later presentation to the psychiatric services[20-22] or they might be because the police treat mentally ill black people differently from their white counterparts.[18]

With one exception,[5] most previous studies have looked retrospectively at hospital admissions alone and have used clinical case note diagnoses.[4 6 12 19] We now report rates of compulsory admission to hospital and contacts with forensic services as part of a wider study to evaluate the prevalence of psychosis and the provision of services among representative cases in two areas of south London.

Patients and methods

A case identification exercise was carried out to establish the annual period prevalence of all psychotic disorders in two catchment areas with 1991 populations of 38 545 and 41 740. Cases were identified by combining data from a wide range of hospital and community sources: psychiatric case records; social services; general practitioners; sheltered accommodation; voluntary, private, and self help care; the clergy; services for the homeless; and prisons. Cases were included on the basis of address of residence, even if no treatment had been received in the index year, and we included both those who had and those who had not ever been in contact with mental health services.

Possible cases were patients who had a clinical diagnosis at any time in their lives of any psychotic disorder. They were rated using the operational criteria checklist version 3.2,[23] a standardised procedure to produce diagnoses according to the 10th revision of the *International Classification of Diseases* (ICD-10).[24] All affective and non-affective functional psychotic disorders were included as definite cases.

For definite cases, information was collected on sociodemographic details, past diagnosis, all contacts with mental health services, use of the Mental Health

PRiSM (Psychiatric Research in Service Measurement), Institute of Psychiatry, De Crespigny Park, London SE5 8AF
Sara Davies, *senior registrar*
Graham Thornicroft, *director and reader*
Morven Leese, *statistician*
Andrew Higgingbotham, *research worker*
Michael Phelan, *assistant director and lecturer*

Correspondence to:
Dr Davies.

BMJ 1996;312:533-7

Act, physical illnesses, family history of mental illness, and contact with the police. Details of compulsory admissions were collected from the Mental Health Act offices of the two local psychiatric hospitals.

Data on ethnic group were collected from a variety of sources. Ethnic group was recorded from the case notes according to the classification system used in the Office of Population Censuses and Surveys 1991 national census.[25] Information was also collected on place and country of birth. When information was not available it was sought from staff who knew the patient. In a random half of all identified cases self rated ethnic group was used to validate the category previously allocated.

Results were analysed with SPSS for Windows, version 6, and STATA (STATA Corporation, Texas, USA). Relative risks were calculated with the white population as the reference group. Confidence intervals were estimated at the 95% level. Pairwise differences in proportions were tested with Fisher's exact test. Interactions tested in addition to main effects were (*a*) between ethnic group and age and (*b*) between ethnic group and whether subjects were born inside or outside the United Kingdom. Risk factors for compulsory detention were analysed by using logistic regression models with forward selection, based on the likelihood ratio, with significance for entry of variables at $P=0{\cdot}05$.

Results

Five hundred and thirty five possible cases with a clinical diagnosis of psychosis were identified in the two sectors. Of these, 439 patients had an ICD-10 psychotic diagnosis as follows: 238 (44·5%) schizophrenia, 13 (2·5%) psychotic affective disorder, and 188 (35·1%) other functional psychotic disorders. These 439 patients are considered to be the representative group of people with psychotic disorders in this study. Five (1·1%) of the patients were found from the community sources alone and had had no contact with mental health services. Sociodemographic characteristics showed that most were single, living in unsupported accommodation, living alone, and not in paid employment (table 1). There were no differences in these characteristics between the sample population and those cases who were excluded because they did not have an ICD-10 diagnosis according to the operational criteria checklist.

In 93·1% of patients ethnic group was established. Of the 194 patients who were subsequently interviewed and who self rated their ethnic group, all agreed with the rating made from the case notes. The ethnic composition of the whole group is shown in table 2. The category "other" comprises three (0·7%) Indian, two (0·5%) Chinese, one (0·2) Asian and nine (2·0%) other ethnic groups; these data were combined for the analyses. The 37 (8·4%) patients whose ethnic origin was unknown were excluded from further analysis. There were no significant differences in the sociodemographic characteristics of the ethnic subgroups, except that the black patients tended to be younger. As there were no significant sociodemographic differences between the black Caribbean and black African patients, and the numbers were small, these were combined into one group of black patients for the analysis of use of specific sections of the Mental Health Act and forensic contact in the study year.

The mean number of admissions was significantly higher for both black Caribbean and black African groups (table 1). Of the whole sample, 229 (51·5%) patients had been placed on a section of the Mental Health Act at some point in their life, and this rate was significantly higher for black Caribbean and black African patients than white patients (table 2).

Differences in risk of sectioning for different age groups are shown in table 3. Logistic regression confirmed the significantly higher risk of ever having

Table 1—*Social characteristics of sample*

Social characteristic	Ethnic group				
	White	Black Caribbean	Black African	Other	Total
Sex:					
Male	126 (49·6)	50 (43·5)	12 (41·4)	8 (53·3)	208 (47·4)
Female	128 (50·4)	65 (56·6)	17 (58·6)	7 (46·7)	231 (52·6)
Age:					
Mean	47·4	35·3	31·2	40·4	42·7
(95% confidence interval)	(45·4 to 49·4)	(32·8 to 37·8)	(27·0 to 35·4)	(31·6 to 49·2)	(41·2 to 44·2)
Age at first contact:					
Mean	29·4	25·76	24·96	25·3	28·1
(95% confidence interval)	(27·6 to 31·2)	(23·8 to 27·7)	(22·4 to 27·5)	(20·1 to 30·5)	(26·9 to 29·3)
Total number of admissions:					
Mean	4·75	4·99	3·04	4·50	4·68
(95% confidence interval)	(4·16 to 5·34)	3·40 to 6·48)	(2·08 to 3·99)	(1·76 to 7·23)	(4·11 to 5·25)
Admissions per year:					
Mean	0·40	0·56	0·84	0·33	0·48
(95% confidence interval)	(0·35 to 0·46)	(0·46 to 0·65)	(0·54 to 1·13)	(0·10 to 0·56)	(0·43 to 0·53)
Marital status:					
Married	63 (24·8)	23 (20·0)	9 (31·0)	2 (13·3)	99 (22·6)
Widowed/divorced	50 (19·7)	12 (10·5)	4 (13·8)	3 (20·0)	74 (16·9)
Single	133 (52·4)	79 (68·7)	15 (51·7)	9 (60·0)	251 (57·2)
Not known	8 (3·1)	1 (0·9)	1 (3·4)	1 (6·7)	15 (3·4)
Accommodation:					
Unsupported accommodation	170 (66·9)	79 (68·7)	19 (65·5)	13 (86·7)	296 (67·4)
Supported accommodation	41 (16·1)	16 (13·9)	0	1 (6·7)	62 (14·1)
Not known	43 (16·9)	20 (17·4)	10 (34·5)	1 (6·7)	81 (18·5)
Living with others:					
Lives alone	95 (37·4)	47 (40·9)	12 (41·4)	5 (33·3)	169 (38·5)
Lives with other	143 (56·3)	61 (53·0)	12 (41·4)	9 (60·0)	235 (53·5)
Not known	16 (6·3)	7 (6·1)	5 (17·2)	1 (6·7)	35 (8·0)
Employment:					
In paid employment	32 (12·6)	19 (16·5)	6 (20·7)	5 (33·3)	64 (14·6)
Not in paid employment	178 (70·1)	84 (73·0)	19 (65·5)	8 (53·3)	302 (68·8)
Not known	44 (17·3)	12 (10·4)	4 (13·8)	2 (13·3)	73 (16·6)
Total (% of whole sample)	254 (57·9)	115 (26·2)	29 (6·6)	15 (3·4)	439 (100)

Table 2—*History of compulsory treatment under Mental Health Act*

Ethnic origin	Patients in sample No (%)	Ever detained under the Mental Health Act No (%)	P value	Relative risk	95% Confidence interval
White:	254 (57·9)	108 (42·5)			
UK born	207	85 (41·1)			
Not UK born	36	18 (50·0)			
Black Caribbean:	115 (26·2)	81 (70·4)	<0·001	1·67	1·39 to 1·99
UK born	58	43 (74·1)			
Not UK born	54	36 (66·7)			
Black African:	29 (6·6)	20 (69·0)	0·01	1·62	1·22 to 2·15
UK born	6	5 (83·3)			
Not UK born	21	14 (66·7)			
Other	15 (3·4)	7 (46·7)	0·79	1·10	0·63 to 1·92
Total	439 (100)	229 (51·5)			

Note that the country of origin was not available for 60 of the patients.
Overall differences between ethnic groups P<0·001; between UK and non-UK born P=0·97 (NS).

Table 3—*Effect of age on differences in rates of ever having been compulsorily detained under Mental Health Act. Values are proportions (percentages) of patients*

Ethnic group	Age group (years)			
	<19	20-39	40-59	>60
White	5/7 (71·4)	40/82 (48·8)	41/100 (41·0)	22/65 (33·8)
Black Caribbean	5/7 (71·4)	55/76 (72·4)	15/23 (65·2)	6/9 (66·7)
Black African	2/2 (100)	14/22 (63·6)	4/4 (100)	0/1 (0)
Overall (white and black)	12/16 (75)	109/180 (61)	60/127 (47·2)	28/75 (37·3)

Trend with age P=0·02, controlling for ethnic group.

Table 4—*Independent effects on risk of having been detained under Mental Health Act 1983*

	Adjusted odds ratio	Confidence interval	P value
Logistic regression model using forward selection			
Black Caribbean	4·46	2·58 to 7·73	<0·001
Black African	3·88	1·45 to 10·37	0·007
Living alone	2·31	1·43 to 3·72	0·006
Total No of admissions	1·13	1·07 to 1·21	0·001
Logistic regression model using forward selection controlling for age			
Black Caribbean	3·67	2·07 to 6·50	<0·001
Black African	2·88	1·04 to 7·95	0·04
Living alone	2·47	1·52 to 4·01	0·003
Age (years)	0·98	0·97 to 1·00	0·02
Total No of admissions	1·15	1·08 to 1·23	<0·001

Based on 342 cases with complete data.

been compulsorily detained for the black groups than for the white patients, and showed a decreasing trend with age. There was no evidence that the trends differed among the different ethnic groups.

Sociodemographic characteristics were considered possible risk factors for sectioning, along with ICD-10 diagnosis and number of admissions, for the logistic regression. The risk factors identified are shown in table 4 with their adjusted odds ratios (black Caribbean and black African group compared with white group, and living alone compared with living with others). Backwards selection resulted in the same selection of risk factors. When the logistic regression model was refitted, controlling for age, the results did not change. The effect of being black Caribbean or black African, taking account of the other significant risk factors for sectioning under the Mental Health Act, was to raise the odds by 3·67 (2·07 to 6·50) and 2·88 (1·04 to 7·95), respectively.

The sections of the Mental Health Act used to detain patients in the study year show that, even though the numbers are very small, the rates of detention of black patients under sections 136, 2, and 3, were significantly higher than those for white patients (table 5). This is most pronounced for section 136. For the other sections, larger proportions of black patients than white patients were detained, but the numbers were small. Results of ever having contact with forensic mental health services (table 6) show that black patients were significantly more likely than white patients to have been admitted at some time in the past to a psychiatric intensive care facility, or to prison.

Discussion

The results indicate that black African and black Caribbean patients are more likely than white patients to have been compulsorily detained in a psychiatric hospital at some time in their lives. This finding is independent of psychiatric diagnosis, total number of admissions a year, age, sex, marital status, employment, living setup, or type of accommodation. They are also more likely than white patients to have been admitted to a psychiatric intensive care unit or to prison.

As far as is known, this is the first study to measure the rates of ever having been compulsorily detained under the Mental Health Act 1983 for a representative group of people with psychosis in a whole catchment area population.

Ethnic groups, as reported in published findings, may fail to show the heterogeneity of such groups,[26 27] but we have justified the categorisations we used in the analysis where the numbers were small. The number of black African patients was small and so their results

Table 5—*Numbers of patients compulsorily admitted under sections of Mental Health Act during study year*

Section of the Mental Health Act	No of patients detained under Act (% of patients in that ethnic group)				P value	Relative risk	95% Confidence interval
	Total (n=439)	White (n=254)	Black (n=144)	Other (n=15)			
5(2)	12	6 (2·3)	6 (4·1)	0			
5(4)	1	0	1 (0·7)	0			
2	40	17 (6·6)	20 (13·9)	3 (20·0)	0·02	2·08	1·12 to 3·83
3	41	17 (6·6)	21 (14·6)	2 (12·5)	0·01	2·18	1·18 to 3·99
4	6	3 (1·2)	3 (2·1)	0			
135	1	0	1 (0·7)	0			
136	16	3 (1·2)	9 (6·3)	0	0·01	5·29	1·46 to 19·23
35	1	1 (0·4)	0	0			
37	6	4 (1·6)	1 (0·7)	0			
37/41	6	3 (1·2)	3 (2·1)	0			

Relative risks for those categories with sufficient data, computed for black patients compared with white patients.
The categories are not mutually exclusive.

Table 6—*Numbers (percentages) of patients ever in contact with forensic services*

	Total (n=439)	White (n=254)	Black (n=144)	Other (n=15)	P value	Relative risk	95% Confidence interval
Previous admission to:							
Special hospital	8 (1·8)	4 (1·6)	3 (2·1)	1 (6·3)			
Secure unit	10 (2·2)	5 (1·9)	4 (2·8)	0 (0)			
Psychiatric intensive care facility	63 (14·4)	25 (9·7)	36 (25·0)	1 (6·7)	<0·01	2·54	1·59 to 4·05
Prison	68 (15·3)	37 (14·3)	29 (20·1)	1 (6·3)	0·16	1·38	0·89 to 2·15

Relative risks for those categories with sufficient data, computed for black patients compared with white patients.
The categories are not mutually exclusive.

need to be interpreted with caution. We principally report here ethnic differences in lifetime ever risk of sectioning for different ethnic groups; other published studies use rates of sectioning under the Mental Health Act 1983 for a specific number of admissions.[8 10 12 13 15 20] The black Caribbean and black African patients described here are younger, and have had contact with services at a younger age than white patients and so they do not have an increased "exposure time." Our study has the further advantage of only counting each individual once so that we avoid the problem of overrepresenting a few individuals who have repeated admissions.

Our findings show a 50% overall risk of ever having been compulsorily admitted to hospital among patients with psychosis. A previous study has shown that for a similar area in south London over a similar time period, 26% of all annual psychiatric inpatient admissions were compulsory, with no difference between ethnic groups, independent of diagnosis.[28]

In a wider context the most recent unpublished figures from the Mental Health Act Commission show that in 1989-90, 7·2% of all admissions to psychiatric hospitals in the United Kingdom were under sections of the Mental Health Act, and of these 4·0%, 1·3%, and 0·8% were under sections 2, 3, and 4 of the Mental Health Act, respectively. This compares in our study with 8·8%, 8·5%, and 1·2%, respectively, in 1992-3, and as our data count individuals, they will underestimate compulsory admission rates. These data do show rates of sectioning in south London that are far higher than the United Kingdom average of a few years ago, and this is confirmed by other recent reports,[29 30] although the reductions in the numbers of available beds nationally means that these figures need to be interpreted cautiously.

This study indicates that independent of diagnosis, black people come into contact with mental health services differently from other groups. Black African and black Caribbean patients are more socially isolated, have greater contact with the police and forensic services, and are more likely to receive involuntary treatment.[6 29 30]

Key messages

- Black patients with psychosis are more likely than their white counterparts to be sectioned under the Mental Health Act
- Black patients are significantly more likely to have been admitted to a psychiatric intensive care facility or to prison
- The differential contact with mental health services may well set up a vicious circle
- Purchasers and providers need to assess how accessible and responsive their mental health services are to black people

Black patients may see mental health services as inaccessible or inappropriate to their requirements.[12] Other recent work suggests that the outcome for black Caribbean and black African patients may be more favourable in terms of risk of self harm and duration of illness despite more involuntary admissions and more imprisonments.[31] This suggests a complex picture.

Whatever the reasons for these higher compulsory admission rates among black patients, this differential experience of contact with services may well establish a vicious circle in which black patients may see services as untherapeutic, may delay seeking help, and will have an increased likelihood of compulsory admission.[28] Purchasers and providers need to address the issue of how accessible and responsive their mental health services are to black people.

We thank Professor Robin Murray and Dr Peter Jones for their helpful comments on an early draft of the manuscript.

Funding: Department of Health.

Conflict of interest: None.

1 Bebbington PE, Hurry J, Tennant C, Sturt E, Wing J. Epidemiology of mental disorders in Camberwell. *Psychol Med* 1981;**11**:561-79.
2 King M, Coker E, Leavey G, Hoare A, Johnson-Sabine E. Incidence of psychotic illness in London: comparison of ethnic groups. *BMJ* 1994;**309**: 1115-9.
3 Castle D, Wessely S, Der G, Murray RM. The incidence of operationally defined schizophrenia in Camberwell, 1965-84. *Br J Psychiatry* 1991;**159**: 790-4.
4 Wessely S, Castle D, Der G, Murray RM. Schizophrenia and Afro-Caribbeans. A case-control study. *Br J Psychiatry* 1991;**159**:795-801.
5 Harrison G, Owens D, Holton A, Neilson D, Boot D. A prospective study of severe mental disorder in Afro-Caribbean patients. *Psychol Med* 1988;**18**: 643-57.
6 McGovern D, Cope R. Second generation of Afro-Caribbeans and young whites with a first admission diagnosis of schizophrenia. *Soc Psychiatry Psychiatr Epidemiol* 1991;**26**:95-9.
7 Bebbington PE, Hurry J, Tennant C. Psychiatric disorders in selected immigrant groups in Camberwell. *Social Psychiatry* 1981;**16**:43-51.
8 Thomas CS, Stone K, Osborn M, Thomas PF, Fisher M. Psychiatric morbidity and compulsory admissions among UK born Europeans, Afro-Caribbeans and Asians in central Manchester. *Br J Psychiatry* 1993;**163**: 91-9.
9 Ineichen B. The mental health of Asians in Britain. *BMJ* 1990;**300**:1669-70.
10 Harrison G, Holton A, Neilson D, Owens D. Severe mental disorder in Afro-Caribbean patients: some social, demographic and service factors. *Psychol Med* 1989;**19**:683-96.
11 Ineichen B, Harrison G, Morgan HG. Psychiatric hospital admissions in Bristol. I. Geographical and ethnic factors. *Br J Psychiatry* 1984;**145**:600-11.
12 McGovern D, Cope R. The compulsory detention of males of different ethnic group, with special reference to offender patients. *Br J Psychiatry* 1987;**150**: 505-12.
13 Owens D, Harrison G, Boot D. Ethnic factors in voluntary and compulsory admissions. *Psychol Med* 1991;**21**:185-96.
14 Turner TH, Ness MN, Imison CT. Mentally disordered persons found in public places. Diagnostic and social aspects of police referrals (Section 136). *Psychol Med* 1992;**22**:765-74.
15 Szmukler GI, Bird AS, Button EJ. Compulsory admissions in a London borough: I. Social and clinical features and a follow up. *Psychol Med* 1981;**11**:617-36.
16 Moodley P, Thornicroft G. Ethnic group and compulsory detention. *Med Sci Law* 1988;**28**:324-8
17 Wessely SC, Castle D, Douglas AJ, Taylor PJ. The criminal careers of incident cases of schizophrenia. *Psychol Med* 1994;**24**:483-502.
18 Littlewood R. Ethnic minorities and the Mental Health Act. Patterns of explanation. *Psychiatric Bulletin* 1986;**10**:306-8.
19 Littlewood R, Lipsedge M. Acute psychotic reactions in Caribbean-born patients. *Psychol Med* 1981;**11**:303-18.
20 Harrison G, Ineichen B, Smith J, Morgan HG. Psychiatric hospital admissions in Bristol II. Social and clinical aspects of compulsory admission. *Br J Psychiatry* 1984;**145**:605-11.
21 Ineichen B. Schizophrenia in British Afro-Caribbeans: two debates confused? *Int J Soc Psychiatry* 1991;**37**:227-32.
22 London M. Mental illness among immigrant minorities in the United Kingdom. *Br J Psychiatry* 1986;**149**:265-73.

23 McGuffin P, Farmer A, Harvey I. A polydiagnostic application of operational criteria in studies of psychotic illness. Development and reliability of the OPCRIT system. *Arch Gen Psychiatry* 1991;48:764-70.
24 World Health Organisation. *Tenth revision of the International Classification of Diseases and related health problems. Clinical Descriptions and diagnostic guidelines.* Geneva: WHO, 1992.
25 Dale A, Marsh C. *The 1991 census user's guide.* London: HMSO, 1993.
26 Senior PA, Bhopal R. Ethnicity as a variable in epidemiological research. *BMJ* 1994;309:327-30.
27 McKenzie KJ, Crowcroft NS. Race, ethnicity, culture and science. *BMJ* 1994;309:286-7.
28 Bebbington PE, Feeney ST, Flannigan CB, Glover GR, Lewis SW, Wing JK. Inner London collaborative audit of admissions in two health districts. II. Ethnicity and the use of the Mental Health Act. *Br J Psychiatry* 1994;165: 743-9.
29 Audit Commission. *Finding a place. A review of mental health services for adults.* London: HMSO, 1994.
30 Fulop N, Koffman J, Carson S. *One-day census of adult acute, low-level secure and elderly mentally ill acute & assessment psychiatric patients across North & South Thames Regions: A report for North and South Thames Regional Health Authorities.* London: HMSO,1995.
31 McKenzie K, van Os J, Fahy T, Jones P, Harvey I, Toone B, Murray R. Evidence for good prognosis psychosis in UK resident people of Caribbean origin. *BMJ* (in press).

(Accepted 23 November 1995)

Serologically diagnosed infection with human papillomavirus type 16 and risk for subsequent development of cervical carcinoma: nested case-control study

Matti Lehtinen, Joakim Dillner, Paul Knekt, Tapio Luostarinen, Arpo Aromaa, Reinhard Kirnbauer, Pentti Koskela, Jorma Paavonen, Richard Peto, John T Schiller, Matti Hakama

National Public Health Institute, Helsinki and Oulu, Finland
Matti Lehtinen, *senior research fellow*
Pentti Koskela, *senior scientist*

Microbiology and Tumorbiology Centre, Karolinska Institute, Sweden
Joakim Dillner, *senior investigator*

Research and Development Centre, Social Insurance Institution, Helsinki, Finland
Paul Knekt, *senior scientist*
Arpo Aromaa, *director of medical research*

Finnish Cancer Registry, Helsinki, Finland
Tapio Luostarinen, *research fellow*

Department of Immunodermatology, University of Vienna Medical School, Vienna, Austria
Reinhard Kirnbauer, *senior research fellow*

University of Helsinki, Finland
Jorma Paavonen, *associate professor of obstetrics and gynaecology*

Clinical Trial Service Unit and ICRF Cancer Studies Unit, University of Oxford, Oxford
Richard Peto, *professor of medical statistics*

Laboratory of Cellular Oncology, National Cancer Institute, Bethesda, Maryland, United States
John T Schiller, *senior investigator*

Tampere School of Public Health, University of Tampere, Tampere, Finland
Matti Hakama, *professor of epidemiology*

Correspondence to:
Dr Lehtinen, Department of Chronic Viral Diseases, NPHI, Mannerheimintie 166, FIN-00300 Helsinki, Finland.

BMJ 1996;312:537-9

Abstract

***Objective*—To study human papillomavirus type 16 in the aetiology of cervical carcinoma.**

***Design*—Within a cohort of 18 814 Finnish women followed for up to 23 years a nested case-control study was conducted based on serological diagnosis of past infection with human papillomavirus type 16.**

***Subjects*—72 women (27 with invasive carcinoma and 45 with in situ carcinoma) and 143 matched controls were identified during the follow up.**

***Main outcome measure*— Relative risk of cervical carcinoma in presence of IgG antibodies to human papillomavirus type 16.**

***Results*—After adjustment for smoking and for antibodies to various other agents of sexually transmitted disease, such as herpes simplex virus type 2 and *Chlamydia trachomatis*, the only significant association was with infection with human papillomavirus type 16 (odds ratio 12·5; 95% confidence interval 2·7 to 57, 2P < 0·001).**

***Conclusion*—This prospective study provides epidemiological evidence that infection with human papillomavirus type 16 confers an excess risk for subsequent development of cervical carcinoma.**

Introduction

Infection with human papillomavirus type 16 (HPV16) is the major factor that has been linked to cervical neoplasia.[1,2] But no prospective studies of infection with human papillomavirus and cervical carcinoma have yet been reported. We have previously reported the risks of cervical carcinoma associated with various other sexually transmitted diseases in a cohort of 18 814 Finnish women followed for 12 years.[3] Only *Chlamydia trachomatis* infection was associated with an increased risk. A recently developed serological assay provides a type restricted measure of infection with human papillomavirus type 16.[4] This and extension of the maximum follow up time to 23 years enabled us (*a*) to determine whether infection is a particularly strong risk factor for subsequent development of cervical carcinoma and (*b*) to determine whether any risk associated with other sexually transmitted infections is independent of the risk associated with exposure to this papillomavirus.

Subjects and methods

Cases and controls were identified as follows. The Finnish Social Insurance Institution carried out a mobile health examination survey among 30 different population groups in various parts of Finland during 1966-72. More than 30 000 women (aged 15 years or more) were invited to a health examination, which included asking about medical history and smoking habits and taking a blood sample. The serum samples of 18 814 women were stored at −20°C.

The population based Finnish cancer registry receives reports of cancer cases from hospitals, pathology laboratories, and physicians throughout Finland. Fewer than 200 cases each of carcinoma in situ (excluding cervical intraepithelial neoplasia) and invasive cervical carcinoma are reported annually. All women who had given blood in the mobile health examination survey during 1968-72 and were free of cancer at the baseline were followed. Those who had cervical carcinoma diagnosed after the baseline examination were identified by linking the data files of the mobile health examination survey and the Finnish cancer registry. Until 1991, 72 cases of cervical carcinoma (27 invasive cervical carcinoma and 45 carcinoma in situ) were diagnosed. Altogether 143 women individually matched for sex, age, and municipality were identified to act as controls. Age was matched by using nearest available matching: in 61 sets the age was exactly matched, in nine sets at least one of the controls differed by one to two years and in two sets by three to four years. Mean (range) age at the baseline was 39·1 (15-83) years and at the diagnosis 49·2 (22-95) years. Mean (range) time (follow up time) between withdrawal of serum and diagnosis of cervical carcinoma was 10·1 (0·7-22·8) years.

IgG antibody analyses were performed by standard enzyme linked immunosorbent assay (ELISA). For human papillomavirus type 16 analysis baculovirus expressed capsids purified by ultracentrifugation and comprising both the L1 and L2 proteins were used with bovine papillomavirus capsids as controls.[4-6] We used *C trachomatis* elementary body to detect chlamydia infection, antigen to lysate from cells infected with herpes simplex virus type 1 for herpes simplex virus, and glycoprotein gG-2 from herpes simplex virus type 2 for herpes simplex virus type 2.[3,7] The same standardised reference serum samples, antihuman IgG enzyme conjugates, and cut off levels were used as in previous studies.[3-7] The specificity of the chlamydia antibodies for *C trachomatis* was confirmed by identifying ELISA positive cases who were microimmunofluorescence positive (> 1:32) for the *C trachomatis* serovars B,E,D/C,J,H,I/G,F,K/ (Washington Research Foundation, Seattle)[8] and for the solely genital *C trachomatis* serovar G,F,K,[9] respectively.